

Investigating Skeletal Muscle Metabolic Adaptations underlying Aerobic Fitness Gains following High Intensity Interval Training in a Rat Model of Pulmonary Arterial Hypertension

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Rationale: In patients with pulmonary arterial hypertension (PAH) a shift from oxidative to a less efficient non-oxidative (glycolytic) metabolism in skeletal muscle is believed to contribute to the reduced exercise tolerance hallmark of the disease. As seen for other cardiopulmonary diseases, exercise training (ExT) may ameliorate this “glycolytic switch” in PAH and improve exercise capacity. Previous studies in this lab showed an improved metabolic profile of skeletal muscle in PAH rats following an ExT protocol of continuous running at moderate relative intensity, 60 minutes at 75% of maximal aerobic capacity (VO₂ Max). This study tests the hypothesis in a PAH rat model that HIIT will also result in preserved aerobic capacity and attenuation of skeletal muscle glycolytic shift. **Methods:** Male Sprague-Dawley rats received either monocrotaline (MCT, 40 mg/kg) to induce mild PAH (n= 14), or saline, for healthy controls (n=9). After 2 wks, a 6 wk program of treadmill HIIT was initiated for a subset of PAH (n= 8) and healthy controls (n=6). The 30 min HIIT sessions alternated between 2 minutes at 85% VO₂ max and 3 minutes at ~30% VO₂ max. VO₂ max was assessed at baseline, and in pre-training and post-training via analysis of expired gases. **Preliminary results:** MCT-induced decrement in VO₂ max was attenuated by HIIT (p<0.05). Soleus muscle hypertrophy (soleus mass relative to body mass) tended to be higher (p=0.07) in HIIT vs. SED MCT. Membrane glucose transporter Glut-1, a marker of glycolytic metabolism, was evaluated in soleus cryosections with immunofluorescent staining and abundance was similar between sedentary and HIIT MCT rats (p>0.05). Western blotting of soleus homogenates for cytochromes I-V of the electron transport chain (OXPHOS), and for PGC1 α , a potent stimulus for mitochondrial biogenesis, is being performed at present to further investigate potential training-induced adaptations in skeletal muscle metabolism

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